In this issue of the *APUA Clinical Newsletter*, we turn our attention to infection control as a powerful means to control increasing spread of more deadly drug-resistant hospital infections worldwide. Our expert authors evaluate individual infection control measures and argue against “component” approaches to infection control programs. They call for better integration of antibiotic stewardship into hospital infection control as the most effective way to slow escalating antimicrobial resistance in all human pathogens. Suggested improvements include: improving AMR surveillance and antibiotic use data collection; improving teamwork within healthcare facilities; and a health systems approach – tracking patient movement throughout the system and among levels and facilities.

The Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) have issued the “Clinical Practice Guidelines for *C. difficile* Infection in Adults” (*Infection Control and Hospital Epidemiology* Vol.31 No.5) which recommends building surveillance tools to track routes of transmission and promoting provider education, accountability, and teamwork among infection preventionists, nursing, and housekeeping staff. Infection control managers should be responsible for ensuring provision of data to unit staff and clinicians and promoting compliance with protocols. At the same time, antimicrobial stewardship efforts – most often led by pharmacy departments – should be integrated with infection control to forestall the emergence of resistant pathogens, thereby lowering the burden for infection control programs. (For more information, see *APUA Clinical Newsletter* Vol.29 No.1, “Antibiotic Stewardship: Recommended Models and Resources.”)

**Optimize Infection Control Using Antimicrobial Stewardship**

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Over the past several years it has become increasingly evident that current infection prevention (IP) initiatives are generally not realizing their hoped-for potential.¹ Although there have been improvements in central line associated bacteremias and class I surgical site infection rates through focused process enhancements, many hospitals continue to experience high rates of *Clostridium difficile* associated infection (CDI), MRSA, and VRE acquisition as well as worsening problems with transmission of resistant Gram-negative pathogens such as *Acinetobacter baumannii*. It is now becoming increasingly evident that broader perspectives and initiatives similar to those which represent the core concepts of antimicrobial stewardship (AS) are urgently needed in the realm of IP.²³

While substantially sequential studies of CDI (1980’s), VRE (1990’s), MRSA (2000’s) and most recently *Acinetobacter* epidemiology were undertaken, there was a failure to optimize broadly effective transmission prevention solutions. Narrowly focused interventions such as using chlorine-based surface disinfectant in *C. difficile* infected patient rooms or the extensive use of isolation for patients colonized but not infected with MRSA and VRE in relatively endemic settings have provided disappointingly little overall impact on infection spread.

**U.S. CDC Guidance on Infection Prevention and Control**

*Arjun Srinivasan, M.D.*  
Associate Director for Healthcare Associated Infection Prevention Programs at the CDC

Want to halt the spread of antibiotic resistance? Think infection prevention. We all know that the best method for preventing antibiotic resistant infections is to limit the overuse and misuse of antibiotics in inpatient and outpatient facilities. Antibiotic stewardship is the cornerstone for CDC’s Get Smart: Know When Antibiotics Work and Get Smart for Healthcare programs. However, what do you do when you find that one of your patients has a drug-resistant infection? How are you going to prevent the infection from spreading to other patients?

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HAI rates. As the importance of each new “pathogen of the decade” became recognized, such narrowly focused interventions were embraced only to be subsequently found to have less impact than had been hoped.

This problem was vividly illustrated in countries that focused on search and destroy interventions to limit the spread of MRSA. While these efforts were successful in containing MRSA transmission in a pre-endemic environment, overall HAI rates in these countries failed to improve during the same time period. Now, a decade later, enteric Gram-negative infections in Great Britain are increasing in the face of focused efforts to control MRSA infections. The belief that we are paying a rapidly escalating price for lost global and local AS opportunities has placed a new emphasis on the need to optimize traditional IP practices. Although the basic IP paradigm is intrinsically simple (Figure 1), effective application of interventions to broadly prevent pathogen transmission have proven to be quite challenging.

Below is an evaluation of individual infection control measures which need to be better integrated to tackle today’s challenges.

Isolation: The intrinsic value of isolation practice has been recognized since ancient times (Figure 1). While screening and single room contact isolation for MRSA colonized patients has increased greatly in recent years, the value of such programs has not been clearly substantiated. In addition, there are substantial challenges related to appropriately determining when to implement and discontinue these logistically complex practices. Furthermore, recent studies have clearly demonstrated their adverse impact on optimal direct patient care, and the increasingly adverse impact on the patient’s emotional well being as well as on hand hygiene.

Hand Hygiene: As the development of alcohol based hand rub (ABHR) products greatly facilitated hand hygiene, there was widespread belief that our collective failure to cleanse our hands before as well as after patient contact was the major factor responsible for ongoing pathogen transmission in healthcare as well as community settings. As a result, there have been extensive, resource intensive efforts to improve hand hygiene compliance. Now, after the publication of more than 2,000 peer-reviewed English language articles over the past 10 years, the great enthusiasm for quickly reaping sub-

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stantial benefits from optimizing hand hygiene practice has been tempered by the realization that acceptance inertia, psychological barriers, suboptimal application technique and particularly the pressures of providing direct patient care can limit the impact of this intervention. As pointed out by Pittet, the latter problem has been shown to be particularly relevant in intensive care unit settings where patient care providers frequently encounter at least 30-40 “hand hygiene moments” an hour, each requiring at least twenty seconds or more to carry out effectively using ABHRs.\(^\text{11}\)

**Environmental Hygiene**: The recently evolving appreciation of the role of surfaces in the transmission of many HAPs (MRSA, VRE, *C. difficile*, *Acinetobacter*, *Pseudomonas*, and others) and many viral pathogens (norovirus, rotavirus, adenovirus, influenza virus) raises the possibility that improving the safety of near-patient surfaces can favorably impact HAP transmission. Although it had been assumed that the cleaning of near patient surfaces (Figure 1) was being optimized in healthcare settings by the use of broadly effective surface disinfectants, recent studies have confirmed non-policy compliant substandard thoroughness of cleaning in essentially all healthcare settings so far studied in the U.S. and abroad.\(^\text{12}\)

Despite the demonstration that improving the thoroughness of traditional cleaning practices through objective monitoring and feedback can significantly decrease acquisition of HAPs such as MRSA and VRE, the impact of sustained improvement in bioburden diminution of near patient surfaces remains to be quantified.\(^\text{13}\) Although optimizing surface microbial cleanliness is likely to have value, there has been a recent explosion of incompletely studied interventions (such as antimicrobial surfaces and semi-automated technologies) that kill/sterilize environmental microbes which are being commercially promoted as “the solution” to the infection transmission problem in healthcare settings.

**Antimicrobial Stewardship**: While the impact of antimicrobial therapy in facilitating antibiotic-specific resistance became vividly evident within a few years of the widespread use of these agents in hospitalized patients, it was not until two decades later that Drs. John McGowen and Maxwell Finland developed a model hospital based antimicrobial stewardship program at Boston City Hospital in the early 1970’s.\(^\text{14}\) Unfortunately, such programs failed to gain widespread acceptance over the next thirty years due to the simplistic hope that the rapid evolution of new therapeutic options would solve “the problem.” Although it appears that the specter of much more widespread and more readily transferable resistance is stimulating greater adoption of hospital-based AS programs, focusing on antimicrobial resistance issues exclusively in hospitals represents only the tip of the iceberg.\(^\text{15}\)

Since its inception 30 years ago, APUA and its leadership have embraced wide perspectives well beyond hospital walls to broadly address AS from the manufacturing process through non-healthcare use issues to optimizing outpatient as well as in hospital prescribing practices. The proponents of APUA’s stewardship perspectives have long advocated a multifaceted simultaneously implemented range of interventions to address resistance issues in which no single component has been considered to be “the answer” or more critical to progress than another. In 1998, John Burke warned of the futility of focusing on a single component of antimicrobial stewardship, which he said was like squeezing a balloon; as you squeeze one area, another pops out.\(^\text{16}\) In the same editorial Burke also pointed to the “perverse and unintended consequences of component management” with respect to AS.

**Conclusions**: It is now becoming increasingly evident that there needs to be a movement away from such “component management” interventions that continue to be serially and independently championed if we are to realize broad-based gains in IP. All the basic components of transmission interventions (Figure 1) need to be seen as mutually critical to broadly optimizing outcomes. As with AS, interventions that advocate any single one of the three basic components of IP practice is really like squeezing a balloon.

As stewardship initiatives have been widely implemented in non-acute care hospital settings, IP interventions similarly and urgently need to move more proactively into these settings. As recent reports have shown, IP initiatives have had significant shortcomings in healthcare settings such as long-term facilities, ambulatory surgical centers, ambulatory dialysis centers, long-term acute care facilities, and even the community.\(^\text{12,17}\) Given the interconnectedness of the microbial world, the likelihood is that a broader, more stewardship-like health systems approach to IP to include these settings will also benefit our most vulnerable hospitalized patients as well as the health of society at large. Unfortunately, the recent explosive dissemination of commensal enteric bacteria with broadly transmissible resistance to all currently available antibiotics clearly places a new sense of urgency on optimizing IP practices as a defense of last resort against such organisms.\(^\text{18}\)

In the context of these perspectives and the escalating problem of antimicrobial resistance to essentially all human pathogens, it is becoming increasingly evident that IP initiatives need to be viewed in a much more global, “stewardship-like” manner. AS and IP need to be seen as inseparable sides of the same coin since both short and long term antimicrobial effectiveness depend on optimization of both of these modalities equally.

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**Figure 1**: Optimizing infection control in healthcare settings.
CDC Guidance continued from page 1

within your ward or healthcare facility?

Recent studies have demonstrated that some of these infections can even spread between communities’ acute care and long-term care facilities. How will you stop this from happening in your community? In short – think infection prevention.

Every year, antibiotic resistance adversely impacts the health of millions of hospitalized patients. We’ve seen that antibiotic resistance can travel the globe. For example, Klebsiella pneumoniae carbapenemase (KPC) infections, a type of resistant carbapenem-resistant Enterobacteriaceae (CRE), were once seen in limited locations in the United States but are now found throughout the country. Those of you who have cared for a patient with a CRE infection know that these organisms are resistant to almost all available antimicrobial agents, and infections from these organisms are associated with high rates of morbidity and mortality. Patients who are critically ill or have been exposed to invasive devices (such as ventilators or central venous catheters) and antibiotics are most likely to be infected with CRE. Fortunately, experience from outbreak investigations and in endemic settings in other countries has suggested that early detection and implementation of strict infection control measures can help control the spread of carbapenem-resistant organisms in healthcare facilities. We often refer to this as a “search and destroy” strategy. In 2009, CDC and the Healthcare Infection Control Practices Advisory Committee released new guidance in an effort to limit the further emergence of CRE in acute care settings. The guidelines recommend several steps:

Start in the laboratory. First, microbiology laboratories in all acute care facilities should implement established protocols to detect carbapenemase production in Enterobacteriaceae, particularly in Klebsiella species or E. coli. If clinical laboratory staff identifies an organism of concern, they should immediately alert hospital infection prevention or epidemiology staff.

Implement contact precautions. When a hospitalized patient with CRE is identified, the most important immediate infection control measure is to implement contact precautions for the patient. Contact precautions require the use of gloves and gowns for patient care.

Search and destroy. If the CRE is thought to have been acquired within the facility – it was not known to be present when the patient was admitted – the guidelines recommend a “search and destroy” strategy through the use of active surveillance among patients who are epidemiologically linked to the case-patient. Active surveillance cultures for CRE can be done through the use of rectal swabs; published protocols are available in the medical literature and in the related links on this page. CRE patients may be in the same unit or may have been cared for by the same healthcare personnel as case-patients. By conducting active surveillance in this manner, you can identify additional patients colonized by these organisms, which can determine whether you have ongoing patient-to-patient transmission of these bacteria in your facility.

If you detect transmission – meaning that you identify cases among patients who epidemiologic links to your case-patient, then infection prevention measures should be vigorously reinforced, and surveillance cultures repeated periodically until no new cases are identified. If no other colonized patients are identified after several instances where surveillance cultures are done on epidemiologically linked patients, it likely means that your facility is effectively controlling transmission. In this circumstance, you may wish to forgo active surveillance in response to new cases of CRE and replace it with periodic point prevalence surveys in units with patients at high risk for CRE infection to ensure that carbapenem-resistant or carbapenemase-producing Klebsiella species and E. coli do not reemerge.

“In some instances, cases of CRE are reported by the microbiology laboratory, but are not detected and acted upon by infection control staff.”

References
Review regularly. In facilities where CRE infections have not been reported, experience also indicates that in some instances, cases of CRE are reported by the microbiology laboratory, but are not detected and acted upon by infection control staff. Hence, to ensure infection control staff has the most accurate information on CRE within their facilities, the guidelines recommend that staff in acute care facilities review microbiology records for the past 6-12 months to ensure that previously unrecognized CRE cases have not occurred.

If you find a previously unrecognized case, it is recommended that you perform some form of active surveillance to determine if there is unrecognized transmission of CRE in your facility. This can be done by conducting a point prevalence survey, which involves performing a single round of active surveillance cultures in units with patients at high risk—such as intensive care units, units where previous cases have been identified, and units where many patients are exposed to broad-spectrum antimicrobial agents. The goal of this survey is to identify any additional patients infected or colonized with carbapenem-resistant or carbapenemase-producing Klebsiella species or E. coli.

Since first being described in North Carolina in 1999, CRE has been found in at least 37 states and are now widespread in some locations. However, we do have an opportunity to act aggressively to halt the spread of CRE. I encourage all of you to review and implement the CDC Guidance for Control of Infections with Carbapenem-Resistant or Carbapenemase-Producing Enterobacteriaceae in Acute Care Facilities.

Experience with CRE suggests that a comprehensive and consistent infection prevention approach can be extremely effective in limiting the transmission of these pathogens. By working together and taking action, we can prevent CRE from becoming a more significant threat to our patients—ultimately improving medical care and saving lives.

Find more of Dr. Srinivasan’s insights on how to develop a strong antimicrobial stewardship program in his article “When It’s Time for an Antibiotic Time Out” (APUA Clinical Newsletter Vol.29 No.1).

Fact sheets from Get Smart: Know When Antibiotics Work on p.8-11.

Prevention of Multidrug-Resistant Organism (MDRO) Emergence and Transmission

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Advanced Measurement Sciences, Clorox Services Company

Basic Facts About MDRO

Multidrug resistant organisms (MDRO) are defined as bacteria that have become resistant to more than one class of antimicrobial agents and usually are resistant to all but one or two commercially available antimicrobial agents, complicating treatment of illnesses they cause.

The emergence of MDRO is increasingly recognized as a major public health threat based on data from the Centers for Disease Control and Prevention (CDC) costing the United States Healthcare system approximately 3.2 billion dollars annually with increasing mortality rates.

Currently, two-thirds of all healthcare-associated infections (HAIs) are caused by just six MDRO referred to by the acronym ESKAPE: Enterococcus species (vancomycin resistant, VRE), Staphylococcus aureus (methicillin resistant, MRSA; intermediate or resistant to vancomycin, VISA/ VRSA), Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species (extended-spectrum beta-lactamase-producing gram-negative bacilli, ESBLs and fluoroquinolone-resistant P. aeruginosa).

MRDO Transmission in Healthcare Facilities

As infection rates of MDRO continue to rise across North America it has become increasingly important to develop more effective infection control programs to reduce the incidence of MDRO-related HAIs. A primary route of MDRO transmission in healthcare facilities is via the hands of healthcare workers. Additionally, however, exposure to contaminated patient-care items or high-touch surfaces such as blood pressure cuffs, toilets, bedside commodes, electronic rectal thermometers, bed rails, call buttons, furniture and improper gloving/glove removal technique have been implicated as infection sources.

Important Elements of an Effective Infection Control Program

Implementation of, and adherence to, infection control practices are key to preventing the transmission of infectious diseases in all healthcare facilities. Recommended practices that should be included in a comprehensive infection control program include, hand hygiene, appropriate antibiotic use, disinfection of the patient environment, standard precautions/ transmission-based precautions, administrative measures, surveillance and education. When followed properly, these practices can decrease MDRO transmission. However, hand hygiene is the single most effective means of preventing the spread of all infections among hospital patients and personnel.

Hand Hygiene: As part of hand hygiene precautions, the following procedures should be followed:

- Wash hands with soap and water when they are visibly dirty or soiled with blood or other body fluids. In doing so, wet hands first with water, apply soap to hands and rub them together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers. Rinse hands with water and dry thoroughly with a disposable towel. Use towel to turn off the faucet.
- If hands are not visibly soiled, an alcohol-based hand rub or gel may be used in place of soap and water. Apply product to the palm of one hand and rub hands together, covering all surfaces of hands and fingers, until the hands are dry.
- Avoid wearing artificial fingernails when caring for patients at high risk for infection, and keep natural nail tips less than 1/4-inch long.
- Wear gloves when contact with blood, mucous membranes, non-intact skin, or other potentially infectious materials could occur. Remove gloves after caring for a patient. Always perform hand hygiene after removing gloves. Never wear the
same pair of gloves for the care of more than one patient. Change gloves during patient care if moving from a contaminated body site to a clean body site.

**Appropriate Antibiotic Use:** The appropriate and prudent use of antibiotics is a key component in controlling MDRO. The CDC provides guidance for judicious use of antimicrobials and tools for implementation. This effort targets all healthcare settings including long term care and focuses on effective antimicrobial treatment of infections, use of narrow spectrum agents, avoiding excessive duration of therapy and restricting use of more potent antibiotics to the treatment of serious infections.²

**Environmental Measures:** The CDC recommends cleaning and disinfecting surfaces and equipment that may be contaminated with pathogens, including those that are in close proximity to the patient and frequently touched surfaces in the patient care environment.²,¹² Although MDRO are resistant to many antibiotics, they are sensitive to properly used Environmental Protection Agency (EPA) - registered disinfectants with claims for the species. Moreover, no data are available that show that antibiotic-resistant bacteria are less sensitive to liquid chemical germicides than the antibiotic-sensitive bacteria at currently used germicide contact conditions and concentrations.²,⁵ During a suspected or proven MDRO outbreak where an environmental reservoir is suspected the following steps should be taken:

- **Routine cleaning procedures should be reviewed along with assessment for need for additional trained cleaning staff.**
- **Adherence should be monitored and reinforced to assure consistent and correct cleaning is performed.**
- **Room cleaning of patients on contact precautions should be prioritized.** Bath tubs, whirlpools, and hydrotherapy tubs should be cleaned and disinfected after each use.

EPA-registered disinfectants or detergents/disinfectants that best meet the overall needs of the healthcare facility for routine cleaning and disinfection should be selected.⁹,¹⁸ These products, which include sodium hypochlorite and quaternary ammonium chloride disinfectants must always be used as recommended by the manufacturer with particular attention being paid to compliance with directions for dilution (if applicable) and contact time with the surface to be disinfected. A list of EPA registered disinfectants may be obtained by calling the National Pesticide Information Center at 800-858-7378 or by visiting http://www.epa.gov/oppad001/chemregindex.htm.

**Standard Precautions/Transmission-Based Precautions:** These require the use of work practice controls and protective apparel for all contact with blood and body substances, and airborne infection isolation, droplet, and contact precautions for patients with diseases known to be transmitted in whole or in part by those routes.²⁰

**Administrative Measures:** Interventions include providing the appropriate number and placement of hand washing sinks and hand sanitizer dispensers, maintaining appropriate staffing levels and enforcing adherence to recommended infection control practices.

**Education:** Patient care and environmental services staff should receive education and training regarding MDRO and the importance of transmis-

**Surveillance:** Surveillance should include maintaining a confidential line listing of residents colonized and/or infected with targeted MDROs. Monitoring culture and antibiotic susceptibility data will help determine baseline rates for MDROs in a facility, indicate the occurrence of increased transmission, and monitor the effectiveness of outbreak control measures.²

MDROs present a unique and growing challenge to healthcare providers and institutions. HICPAC recommends fastidious environmental cleaning and disinfection of patient care items and environmental surfaces to reduce bacterial load and risk of transmission.⁶,¹⁴ Additionally, good antimicrobial stewardship complements infection control efforts and environmental interventions to provide a more comprehensive strategy to prevent and control outbreaks of MDROs. Successful outcomes are usually based on a combination of the multiple interventions outlined above.¹²,¹⁴,¹⁶

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EPA-registered to kill *Clostridium difficile* spores in 5 minutes*

- Proven to kill *C. difficile* spores, supported by clinical studies.
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bacteria and transfer a dominant gene called rpsL that confers renewed sensitivity to certain antibiotics. After preclinical animal trials, this cost-effective tellurite compound can then be added to cleaning supplies to be used in hospitals and other medical facilities.


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### New Research

**New Reports on Antimicrobial Resistance**

**Alison Moore, B.A. APUA Staff Reporter**

**New cleanser may help reverse antibiotic resistance**

Dr. Udi Qimron of the Department of Clinical Microbiology and Immunology at Tel Aviv University's Sackler Faculty of Medicine has developed a liquid solution based on specially designed bacteriophages to help fight antibiotic-resistant bacteria. These bacteriophages are engineered to infect
Delivering safe care for patients: all healthcare providers play a role

Did you know?
1. Antibiotic resistance is one of the world’s most pressing public health threats.
2. Antibiotics are the most important tool we have to combat life-threatening bacterial diseases, but antibiotics can have side effects.
3. Antibiotic overuse increases the development of drug-resistant germs.
4. Patients, healthcare providers, hospital administrators, and policy makers must work together to employ effective strategies for improving antibiotic use – ultimately improving medical care and saving lives.

Scope of the Problem
Today, infections with antibiotic-resistant bacteria have become increasingly common in healthcare and community settings. Antibiotic resistance occurs when germs change in a way that reduces or eliminates the effectiveness of the drugs available to treat them. Many bacteria have now become resistant to more than one type or class of antibiotic and widespread overuse and inappropriate use of antibiotics is fueling resistance that compromises the effectiveness of important patient treatments. Overuse of antibiotics also increases the problems of drug side effects, allergic reactions, diarrheal infections caused by Clostridium difficile, or even death.

Inpatient Settings
- Antimicrobial resistance adversely impacts the health of millions of hospitalized and patients every year.
- Of the patients receiving antibiotics, half (50%) will receive unnecessary or redundant therapy, resulting in overuse of antibiotics.
- Unnecessary use of antibiotics creates risk of adverse drug events and Clostridium difficile with no benefits to patients. C. difficile is a serious diarrheal infection and is on the rise.
- Some infections in hospitals are now resistant to all available antibiotics.

Outpatient Settings
- Each year, tens of millions of antibiotics are prescribed unnecessarily for viral upper-respiratory infections.
- In states where there is more antibiotic use, there are more antibiotic-resistant pneumococcal infections.
- Antibiotic use in primary care is associated with antibiotic resistance at the individual patient level.
- The presence of antibiotic-resistant bacteria is greatest during the month following a patient’s antibiotic use and may persist for up to 12 months.
Why we must act now
- The way we use antibiotics today or in one patient directly impacts how effective they will be tomorrow or in another patient; they are a shared resource.
- Antibiotic resistance is not just a problem for the person with the infection. Some resistant bacteria have the potential to spread to others—promoting antibiotic-resistant infections.
- Since it will be many years before new antibiotics are available to treat some resistant infections, we need to improve the use of antibiotics that are currently available.

Healthcare providers can
**Prescribe correctly**
- Refrain from treating viral syndromes with antibiotics, even when patients ask for them.
- Prescribe the right antibiotic at the right dose for the right duration; be familiar with resistance trends in your region.
- Avoid unnecessary overlaps in antibiotics. It is not usually necessary to give two antibiotics to treat the same bacteria.

**Collaborate with each other and with patients**
- Talk to your patients about appropriate use of antibiotics.
- Include microbiology cultures when placing antibiotic orders.
- Work with pharmacists to counsel patients on appropriate antibiotic use, antibiotic resistance, and adverse effects.
- Utilize patient and provider resources offered by CDC and other professional organizations.

**Stop and assess**
- Take an “antibiotic timeout” when a patient’s culture results come back in 24 to 48 hours. Stop and assess the use of antibiotics, using them only when indicated to avoid promoting the development of resistance among bacteria and unnecessary antibiotic exposure.

**Embrace antibiotic stewardship**
- Improve antibiotic use in all facilities—regardless of size—through stewardship interventions and programs, which will improve individual patient outcomes, reduce the overall burden of antibiotic resistance, and save healthcare dollars.
- Recognize and participate in the United States’ fourth annual Get Smart about Antibiotics Week, November 14-20, 2011, an international collaboration that coincides with Canada’s Antibiotic Awareness Week and European Antibiotic Awareness Day on November 18, 2011.
Antibiotic stewardship – the ultimate return on investment

Get Smart About Antibiotics Week
Wednesday, November 16, 2011

Did you know?
1. Antibiotic resistance is one of the world’s most pressing public health threats.
2. Antibiotics are the most important tool we have to combat life-threatening bacterial diseases, but antibiotics can have side effects.
3. Antibiotic overuse increases the development of drug-resistant germs.
4. Patients, healthcare providers, hospital administrators, and policy makers must work together to employ effective strategies for improving antibiotic use – ultimately improving medical care and saving lives.

Save money with antibiotic stewardship

Antibiotic stewardship programs and interventions help ensure that patients get the right antibiotics at the right time for the right duration. Numerous studies have shown that implementing an antibiotic stewardship program can not only save lives, but can save significant healthcare dollars. Inpatient antibiotic stewardship programs have consistently demonstrated annual savings to hospitals and other healthcare facilities of $200,000 to $400,000.

- According to a University of Maryland study, implementation of one antibiotic stewardship program saved a total of $17 million over 8 years at one institution.
  - After the program was discontinued, antibiotic costs increased over $1 million in the first year (an increase of 23 percent) and continued to increase the following year.
- In a study conducted at The Johns Hopkins Hospital, it was demonstrated that guidelines for management of community-acquired pneumonia could promote the use of shorter courses of therapy, saving money and promoting patient safety.
- Targeting certain infections may decrease antibiotic use. For example, determining when and how to treat patients for urinary tract infections, the second most common bacterial infection leading to hospitalization, can lead to improved patient outcomes and cost savings.

Antibiotic stewardship programs are a “win-win” for all involved.
- A University of Maryland study showed one antibiotic stewardship program saved a total of $17 million over 8 years.
- Antibiotic stewardship helps improve patient care and shorten hospital stays, thus benefiting patients as well as hospitals.
Why we must act now

- The way we use antibiotics today or in one patient directly impacts how effective they will be tomorrow or in another patient; they are a shared resource.
- Antibiotic resistance is not just a problem for the person with the infection. Some resistant bacteria have the potential to spread to others – promoting antibiotic-resistant infections.
- Since it will be many years before new antibiotics are available to treat some resistant infections, we need to improve the use of antibiotics that are currently available.

Promote antibiotic best practices – a first step in Antibiotic Stewardship:
1. Ensure all orders have dose, duration, and indications
2. Get cultures before starting antibiotics
3. Take an “antibiotic timeout,” reassessing antibiotics after 48-72 hours

Healthcare facility administrators and payers can

- Make appropriate antibiotic use a quality improvement and patient safety priority.
- Focus on reducing unnecessary antibiotic use, which can reduce antibiotic-resistant infections, reduce Clostridium difficile infections, and reduce costs, while improving patient outcomes.
- Emphasize and implement antibiotic stewardship programs and interventions for every facility – regardless of facility setting and size.
- Monitor Healthcare Effectiveness Data and Information Set (HEDIS®) performance measures on pharyngitis, upper respiratory infections, acute bronchitis, and antibiotic utilization.

Antibiotic Stewardship in your facility will:
- Decrease antibiotic resistance
- Decrease C. difficile infections
- Decrease costs
- Increase good patient outcomes

Centers for Disease Control and Prevention
For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (1-800-432-4636) TTY: 1-888-232-6354
Email: cdcinfo@cdc.gov  Web: https://www.cdc.gov/antibiotic/  Web: https://www.cdc.gov/antibiotic/whatiswork/
Visualizing the progression of antibiotic resistance

The Center for Disease Dynamics, Economics & Policy (CDDEP) created an interactive map visualizing antibiotic use and highlighting trends in outpatient prescribing in the US. In 2007 the average number of dispensed outpatient antibiotic prescriptions per 1,000 inhabitants at the national level was 858, or 0.86 prescriptions per person. There are large regional variations in utilization rates, ranging from 0.55 dispensed prescriptions per person in Alaska to 1.22 dispensed prescriptions per person in West Virginia. All classes of prescribed antibiotics follow a common regional pattern with states in and around the East South Central region (West Virginia, Tennessee, Kentucky, Mississippi, Alabama, Arkansas, and Louisiana) getting nearly twice as many prescriptions as Pacific states, and more than 15% of all use nationally. Try using ResistanceMap interactively at http://www.cddep.org/ResistanceMap/use.


Review: key steps in controlling antibiotic resistance

A group of scientists (including APUA Scientific Advisory Board members Patrice Courvalin, Julian Davies, George Jacoby, Stephen Lerner, Stuart Levy, Alexander Tomasz) led by Shahriar Mobashery of the University of Notre Dame has published a paper outlining key steps that need to be taken to control the global crisis of antibiotic resistance. The group notes that in Europe in 2007, 400,000 infections and 25,000 deaths were attributed to multidrug-resistant bacteria. Antibiotic resistant infections cost the United States $20 billion per year in excess healthcare costs, $35 billion per year in societal costs and $8 million additional hospital stays per year.

The group called for established research priorities, increased international funding, encouragement and support of local governments to establish better infrastructure, tighter regulation of antibiotics, and incentives to develop new antibiotics.


Three infection control interventions to save lives and cut costs

University of North Carolina at Chapel Hill researchers led by Bradford D. Harris found that improving practices of hand hygiene, ventilator and oral care, and central-line catheter care led to dramatic reductions in infections (especially ventilator-associated pneumonias and central-line-associated bloodstream infections), mortality, and hospital costs. Results of the study showed that patients admitted after these interventions were implemented shortened their hospital stay by an average of two days and cut their cost by $12,000, while the number of patient deaths was reduced by 2.3%. These interventions were also cost effective, costing around $21 per day for oral care kits and $0.60 per day for antisep tic patches and hand sanitizers. If replicated nationwide, these interventions have the potential to save thousands of lives and billions of dollars each year.


Obituaries

It is with great sadness that we inform you of the passing of one of APUA’s esteemed colleagues. On October 17, 2011, Dr. Alexander Nanuashvili (APUA-Georgia President) passed away after a brief illness. His tireless efforts with APUA-Georgia generated admiration and respect from his colleagues and others concerned with the prudent use of antibiotics. He was affiliated with the Infectious Diseases Department of the Tbilisi Medical Academy of Postgraduate Education in Tbilisi, Georgia. He is survived by his wife Dr. Tamar Davitashvili (Center for Infectious Pathology) and three children. We will miss him dearly.

APUA-Georgia was founded in February of 2003 in affiliation with the Service of Antimicrobial Chemotherapy by the members of the Infectious Disease Department of Tbilisi Medical Academy. On May 31, 2008, APUA-Georgia presented national guidelines for the management of bacterial meningitis and nosocomial pneumonia at the APUA-Georgia conference. In addition, APUA-Georgia has recently conducted important studies on MRSA in children, the antimicrobial activity of polymyxin B against non-fermentative Gram-negative bacteria, and ESBL in Georgia. APUA-Georgia owes much to Dr. Nanuashvili’s legacy.

Transitions

Dr. Anibal Sosa, who has provided valuable service over many years as director of the APUA International Chapter Program, has left APUA to pursue other professional opportunities as of Sept 29, 2011. APUA is continuing its active program of chapter services. For chapter questions and issues, please contact Kathleen Young (kathleen.young@tufs.edu) or Bonnie Marshall (bonnie.marshall@tufs.edu), who is serving as active liason. Bonnie has worked closely with Dr. Levy for many decades and has played a key technical role with chapters on several large surveillance projects funded through APUA.
APUA-Cuba Chapter News

Moisés Morejón, M.Sc.
Manuel Fajardo Hospital
APUA-Cuba President

APUA-Cuba recently took part in two large-scale conferences on antimicrobial use issues, both within Cuba and throughout the region of Latin America. The first conference was the National Workshop on Antibiotic Resistance, which was sponsored by APUA-Cuba and took place in the Cuban municipality of the Isla de la Juventud from October 13 to October 15, 2011. Over 100 representatives from 11 hospitals and research institutions throughout the country were present, holding symposia, panel discussions, and round table discussions focused on raising national awareness of the issue of antibiotic resistance and proposing counterstrategies. The participating institutions summarized their findings into a document called the Nueva Gerona Declaration on Antimicrobial Resistance.

The Nueva Gerona Declaration took as its motto the slogan of World Health Day 2011 – “Si no actuamos hoy, no habrá cura mañana (No action today, no cure tomorrow).” The Declaration called all Cuban scientists and health professionals to work together to promote, implement, and oversee programs and government policies geared towards the rational and prudent use of antibiotics. It also emphasized necessary steps such as: 1) promoting education about antibiotic resistance among healthcare professionals as well as in the patient population, 2) improving laboratory capabilities and diagnostic technology, 3) scrutinizing and regulating the use of critically important antibiotics, 4) collaborating between and within healthcare facilities and their subdivisions (e.g. pharmacy, clinical laboratories, microbiology laboratories), and 5) promoting preventative measures such as hand hygiene.

APUA-Cuba also attended the workshop “Antimicrobials for Veterinary Use,” sponsored by the Cuban Ministry of Public Health, and gave the first lecture there on “The Global Landscape of Infectious Disease: the Situation in Cuba.” Dr. Moisés Morejón (APUA-Cuba President) spoke about the close relationship between human and animal health and the rise in food-borne illness caused by *Staphylococcus*, especially those caused by multidrug-resistant staphylococci (MRSA) found in both food animals and the food industry personnel who work with them. He emphasized that the misuse of antibiotics in agriculture and food animal production is contributing to the danger of food animals becoming reservoirs of MRSA and other resistant bacteria.

Dr. Ana Granda (of the National Center for Nutrition and Food Hygiene) spoke about the need for surveillance to predict the emergence of resistant strains of bacteria around the world, and Dr. Marieta Sonali (also of the National Center for Nutrition and Food Hygiene) spoke about the emergence of foodborne disease as a growing global health problem and the need for improved food safety policies “from farm to fork” throughout Latin America. Dr. Emigdio Lemes (Drug Registration Office of the Institute of Veterinary Medicine) introduced his newly approved national project entitled “Procedures for the Responsible and Prudent Use of Antimicrobials in Veterinary Medicine in Cuba,” which proposes a ban on antibiotics as growth promoters in food animals as well as a ban on using human antibiotics in animal production. The workshop culminated with the founding of a sub-chapter of APUA-Cuba, APUA-Cuba Veterinary, to develop guidelines for the appropriate use of antibiotics in humans and animals.

APUA-Cuba has worked tirelessly throughout 2010 and 2011 and has established five sub-chapters in different parts of the country. Today, their membership is 1070 members and still growing.

APUA-Argentina Chapter News

Gustavo Lopardo, M.D.
Prof. Dr. Bernardo Houssay Hospital
APUA-Argentina President

A brief communication by APUA-Argentina entitled “Antimicrobial Stewardship Programs in a Developing Country: The Epidemiological Barrier” was recently accepted by the Pan-American Journal of Public Health (the official publication of PAHO) and is pending publication. The authors are Dr. Gustavo Lopardo (APUA-Argentina President) and his colleagues from the Hospital Prof. Dr. Bernardo Houssay and the Instituto Sacre Coeur, both in Buenos Aires.

The paper describes the process of developing an antibiotic stewardship program (ASP) in a 140-bed university hospital in Argentina. The authors recognize the benefits of an established ASP – improved clinical outcomes through reduced emergence of resistance, limited drug-related adverse effects, and limited healthcare-acquired infections. In Phase 1 of ASP development (2007-2008), the investigators implemented strict restriction policies (requirement of an infectious disease physician’s approval before any attending physician can prescribe certain antibiotics) as well as supplemental policies. In Phase 2 of development (2008-2009), the investigators stopped using restriction policies and relied only on supplemental policies of antibiotic
stewardship, such as having pharmacists review prescriptions every day, giving feedback about antibiotic usage to physicians, facilitating bedside discussion about antibiotic therapy between physician and patient, and implementing the active presence of three ID physicians throughout the hospital for six hours a day.

Comparing antibiotic usage between Phase 1 and Phase 2 of ASP development revealed that some antibiotics were prescribed significantly less in Phase 2, some antibiotics were prescribed more, and some exhibited no change. The antibiotics prescribed more during Phase 2 were mostly given in the ICU in response to multidrug-resistant infections. It seemed that despite implementing both core and supplemental policies of antibiotic stewardship, other factors were capable of worsening and spreading the problem of antibiotic resistance — such as invasive measures and infection prophylaxis under inadequate hygiene standards.

The investigators concluded that infection control is most successful when it integrates vigilant hygiene (to prevent the survival and transfer of resistant bacteria) with individual assessments of a hospital or clinic’s circumstances, which might call for additional measures such as patient isolation and staff cohorting. They also acknowledged that hospitals in developing countries may lack the infrastructure to implement such measures consistently and effectively, and recommended that health authorities in those countries should promote antibiotic stewardship programs and other infection control measures. Look for the full text of Dr. Lopardo’s article and detailed study methods in the Pan-American Journal of Public Health.

APUA-Bulgaria Chapter News
Emma Keuleyan, M.D., Ph.D.
Medical Institute of the Ministry of the Interior
APUA-Bulgaria Coordinator

Dr. Rossitza Vatcheva-Dobrevska (Head of the National Reference Centre for Healthcare-Associated Infections) and Dr. Emma Keuleyan (APUA-Bulgaria President) gave an overview of infection control measures being implemented in Bulgaria. The incidence of healthcare-associated infections (HAIs) dropped from 12.7% in 2007 to 11.2% in 2008, and 10.2% in 2009. Over the past five years, the recorded incidence decreased by approximately 3%. From 1999 to 2009, the incidence decreased by approximately 10% (21.1% to 10.2%). In a national point prevalence survey conducted in 2006 among 23 acute-care hospitals in Bulgaria, the overall prevalence rate of HAI was 2.43%. Highest prevalence rates were found in intensive care units (15.2%) and surgical wards (4.1%). Of all HAIs, the most common types were surgical site infections (43.18%), pneumonia (27.27%), urinary tract infections (20.45%), and primary bloodstream infection (9.09%). Dr. Keuleyan cites lack of resources within current practice to handle antimicrobial resistance within hospitals.

APUA-Bulgaria shares national responsibility with the Ministry of Health, the National Center for Infectious and Parasitic Diseases (NCIP), the National Reference Center for Healthcare-Associated Infections (NRC-HAI), and the National Centre for Public Health and Information (NCPHI) for infection control activities. Bulgaria has also participated in a series of ECDC surveys of HAIs, such as the European Clostridium difficile infection surveillance network project (ECDIS-net), as well as a national campaign for hand hygiene. The hand hygiene campaign included an evaluation of existing resources and standards within hospitals as well as a survey of patient knowledge. For World Health Day 2011 the poster reads, “Let’s Stop Antimicrobial Resistance! ESBLs (broad-spectrum β-lactamases) cause resistance towards combinations of antibiotics - let’s stop them!”

Poster publicizing World Health Day 2011

7-я април - международен ден на здравето
Да спрем антибиотиканата резистентност!
ESBL - широк спектър β-лактамази, ги устойчивост към комбинация от антибиотици - да ги спрем!
APUA-Croatia Chapter News
Arjana Tambic Andrasevic, M.D., Ph.D.
Zagreb University Hospital for Infectious Diseases
APUA-Croatia President

APUA-Croatia has seen rates of MRSA decrease from 23% in 2006 to 15% in 2010. Incidence of MRSA also decreased from 66/1000 bed days in 2007 to 12/1000 bed days in 2010. At the same time, rates of P. aeruginosa have been continually high (26% in BSI and 12% in clinical isolates) and carbapenem resistance has increased (34% in 2010). Dr. Smilja Kalenic (National Committee for Nosocomial Infection Control) and Dr. Arjana Tambic Andrasevic (APUA-Croatia President) report that though there are several active infection control activities occurring in Croatia, resistance levels are still high in hospitals.

While all hospitals in Croatia have infection control committees and infection control nurses, Dr. Kalenic and Dr. Andrasevic note that not all have satisfactory operating infection control teams. Other areas for improvement include outcome indicators, antibiotic consumption in hospitals, antibiotic stewardship programs, and the lack of national intervention strategies to support local infection control team efforts.

Within Croatia, many strategic partnerships have evolved. The Croatian Ministry of Health and Social Welfare (MHSW) Reference Center for Antimicrobial Resistance Surveillance at the University Hospital for Infectious Diseases. Croatia also began a campaign targeting hospital antibiotic use in 2010, on the recommendation of the ECDC. Various national symposia are also held to commemorate European Antibiotic Awareness Day and Hand Hygiene Day. APUA-Croatia also takes part in ongoing education programs, including a poster presented by APUA-Croatia and partners for a national hand hygiene campaign.

Day on April 7, 2011, APUA-Bulgaria collaborated with the Bulgarian Association of Microbiologists and the Medical Institute of the Ministry of the Interior to produce a poster about broad-spectrum β-lactamases (ESBLS).

Over the next few years, Bulgaria will focus on implementation of the Medical HAI Standard, the Program for HAI Prevention and Control, and the control of antimicrobial resistance. Goals include harmonization of national practical standards for infection prevention and control with European standards. Practical implementation in health care facilities will include measures for improving patient and personnel safety, containment of HAIIs and AMR, and a better understanding of the scope and consequences of HAIIs in the medical community and society. Future activities include participation in the ECDC European Point Prevalence Survey of HAI and Antimicrobial Use in European Acute Care Hospitals for 2011-2012, and the introduction of the new ECDC protocols for active HAI surveillance in hospitals to allow participation in the ECDC HAI-NET.
Coalition letter to U.S. Congress on the state of the science

On September 6, 2011, a coalition of public health organizations led by the Pew Health Group wrote a letter to Congress on the state of the science regarding the use of antibiotics in food animals. Assertively titled “Sound Science: Antibiotic Use in Food Animals Leads to Drug Resistant Infections in People,” the letter repudiated claims made on the House floor that there is a lack of “hard” scientific evidence for a link between inappropriate antibiotic use in food animals and human antibiotic resistance.

The coalition cited repeated testimonies from the USDA, FDA, and CDC stating that the use of antibiotics in food animals is resulting in the presence of resistant strains in the food supply that can be readily transmitted to consumers. The organizations also referred to reports by the Government Accountability Office, the Institute of Medicine, WHO, the World Organization for Animal Health, and the Food and Agriculture Organization of the UN that affirmed “clear evidence of adverse human health consequences” from the use – especially at subtherapeutic levels such as those used in growth promotion – of antibiotics in animal agriculture. They also cited examples of the scientific studies conducted as early as 1984 and as recently as 2010 that provided this evidence.

Organizations that signed on to this letter with the Pew Health Group included APUA, the American Medical Association, the American Public Health Association, the Infectious Diseases Society of America, the Johns Hopkins School of Public Health, and many other leaders in the fields of public health and epidemiology. APUA was also proud to canvass individual support for the letter at the 49th annual meeting of the IDSA held in Boston, MA from October 20 to October 23, 2011. Find the full text of the letter and the complete list of coalition members at saveantibiotics.org.

NIAA symposium on animal agriculture instigates dialogue among stakeholders

The National Institute for Animal Agriculture (NIAA) conducted a symposium entitled “Antibiotic Use in Food Animals: A Dialogue for a Common Purpose” from October 26 to October 27, 2011, in Chicago, IL. The stated goal of the symposium was “One Health: Healthy People, Healthy Animals, Healthy Food,” and it convened 13 animal health and human health scientists to speak on four main topics: 1) human health implications relative to antibiotic use, 2) regulatory oversight and risk mitigation, 3) livestock-associated MRSA (understanding and communicating the risks), and 4) connecting with consumers.

For each topic, the dialogue focused on finding areas of consensus and discussing science-based vs. value-based agreements and disagreements. Carol Cogliani (APUA Public Policy Director) was present, and 151 participants (representatives of animal agriculture, veterinary medicine, the pharmaceutical industry, and the media) attended.

On one side of the dialogue, some representatives of animal agriculture and pharmaceutical representatives claimed that antibiotic use in food animals is already sufficiently regulated by the FDA Center for Veterinary Medicine to ensure that no harmful residues enter the food supply. They stated that the risk to human health from on-farm antibiotic use was lower than the alternative risk of having suboptimal animal health, and that the measurable adverse consequences to human health from antibiotic use in food animals (e.g. days of hospitalization due to antibiotic-resistant infection) are either unknown or very low.

Food animal producers also denied that livestock-associated methicillin-resistant Staphylococcus aureus (LAMRSA) contributes significantly to the overall presence of MRSA in humans, or is a foodborne pathogen at all. Rather than the use of antibiotics in food animals, they cited large hospitals, the co-hospitalization of children and the elderly, and increasing travel as factors that might be responsible for rising levels of antibiotic-resistant bacteria.

Some factors that food animal producers brought up in the dialogue to defend their on-farm antibiotic use practices were that livestock farms consult closely with veterinarians on health management decisions, that sick animals must be treated with antibiotics to restore their health and ensure that their milk and meat is safe for consumption, and that once undergoing antibiotic treatment the animal or animal product is not allowed to enter the food supply until the drug has sufficiently cleared the animal’s system. They acknowledged that biosecurity measures and the use of vaccines could help minimize the need for antibiotics, and that medically important antibiotics should only be used as drugs of last resort under the supervision of a veterinarian on a case-by-case basis.

The opposing viewpoint, from clinical microbiologists and other public health representatives, stated that dosage and duration of antibiotic therapies (such as administering antibiotics at low doses in animal feed over long periods as a growth promoter) do alter the selective pressure on bacteria that cause some strains to become resistant. They cited globally increasing resistance rates of many pathogens to many classes of antibiotics, including the tetracyclines, cephalosporins, and carbapenems (currently the “last line” of antibiotic drugs). Microbiologists also brought up the issue of the horizontal transfer of genetic resistance elements between bacteria via transposons, which highlights the danger of antibiotic resistance passing from food animals to industry personnel and from there into the populace, even if the resistant bacteria is not found on retail meat and the general population never comes into contact with the live animal.

Food animal producers stated that as industry grows, farms are forced to produce more animals and thus use more antibiotics to ensure the health of large herds. In response, some farmers of smaller farms advocated that there is a niche market in which consumers will pay for local animals raised by alternative animal husbandry practices rather than by antibiotic use. They suggested...
Many representatives described great stewardship programs at their hospitals. The concluding speaker for the symposium was Dr. Mike Lormore of Pfizer Animal Health. While he maintained that the risk to human health from antibiotic use in animals is still unknown, he did emphasize the need for food animal producers to maintain standards and lower antibiotic residues in food products. He also recommended that producers take on more protocols ensuring appropriate antibiotic use and a greater degree of veterinary oversight. In addition, he stressed the need for producers to communicate truthfully with consumers about why antibiotics are being used and how much.

**APUA co-sponsors conference “Building Stewardship: A Team Approach”**

“Building Stewardship: A Team Approach” was an educational conference held on September 14, 2011, to educate healthcare professionals about the implementation and optimization of antibiotic stewardship in acute care hospitals. Held in Shrewsbury, MA, the conference was co-sponsored by APUA, the Massachusetts Department of Public Health, the Massachusetts Coalition for the Prevention of Medical Errors, Tufts Medical Center, UMass Memorial Medical Center, and Brigham and Women’s Hospital.

The conference featured presentations on strategies for building and implementing antibiotic stewardship programs, followed by smaller group sessions on pharmacodynamics and kinetics, hospital team planning, business plans, and models for program evaluation and IT metrics. A follow-up audioconference was held on November 10, 2011, in which representatives from the 38 healthcare facilities that had attended the conference were invited to report on the efforts they had made since the conference to create or improve antibiotic stewardship programs at their hospitals. Many representatives described great strides in creating and updating antibiograms and antibiotic audit reports to document all relevant data about an antibiotic therapy (such as type, dose, duration, and mode of administration), often making use of software such as Vitek and WHONET. They also expanded the stewardship programs at their institutions to include not only infectious disease physicians but also ID nurses, pharmacists, and microbiology labs, all vital elements to an effective program. There was also great interest from hospitals in acquiring PCR capability to rapidly identify pathogens such as MRSA and C. difficile, and get their resistance and susceptibility data.

For the future, representatives suggested implementing formularies at their hospitals to restrict the use of certain antibiotics. They were also all in favor of better interdepartmental communication, in which close collaboration between physicians and pharmacists will facilitate appropriate selection and dosing of antibiotics and streamline the labor-intensive processes of IV to PO transition and de-escalation. Another strategy was establishing a decentralized committee of ID physicians or pharmacists who can be scattered throughout a hospital, so that each expert is responsible for fewer patients and has higher accountability.

The audioconference generated many practical guidelines to help hospitals develop the best possible antibiotic stewardship programs for their circumstances. Gathering representatives after the conference to talk about their progress and give each other suggestions was very effective, and provided insights that were reiterated later in the month during the national campaign Get Smart About Antibiotics Week.

**APUA poster on African research**

The 49th Annual Meeting of the Infectious Disease Society of America (IDSA) and the HIV Medicine Association were held in Boston, Massachusetts on October 20-23, 2011. The APUA poster featured research from Dr. Susan Foster, Dr. Anibal Sosa, and Dorothy Ochieng in a poster based on findings from an African field study funded by the Gates Foundation, enti-


In Uganda, APUA researchers found that many children diagnosed with pneumonia in an outpatient setting were prescribed the antibiotic co-trimoxazole (to which the rate of resistance approaches 80% in that country), multiple antibiotics, or no antibiotic at all. As a result, antibiotic therapy was potentially ineffective or absent in about 37% of cases. In addition, children with a pneumonia diagnosis were almost as likely to receive an antimarial (58%) as an effective antibiotic (63%). Rising rates of resistance to benzyl penicillin and amoxicillin were also observed.

In Zambia, despite lack of surveillance and reliable diagnostics, APUA researchers identified *S. pneumoniae* as a primary pediatric pathogen for acute respiratory infections. Based on antibiotic resistance trends, ampicillin plus gentamicin were recommended as the best treatment option for severe pneumonia, and Short-Course Home Oral Therapy (NO-SHOTS) of pneumonia with amoxicillin seemed to be a better option than injectable penicillin.

The goal of this and other IDSA presentations was to increase awareness of rising levels of antibiotic resistance, and the global need for new antibiotics. APUA representatives Jennie Choe, Samantha Graham, and Alison Moore staffed the APUA exhibit, distributed educational material, and networked with interested health professionals.

**APUA partners with CDC for Get Smart Week 2011**

APUA was an active strategic partner in the U.S. CDC’s annual Get Smart About Antibiotics Week (held from November 14 to November 20, 2011), collaborated with the CDC by posting educational brochures, podcasts, and other materials at www.apua.org. APUA also contributed expert opinions to CDC’s live Twitter chat, hosted by ABC’s Dr. Richard Besser, about upper respiratory tract infections, appropriate antibiotic use, and antibiotic resistance. The goal of the event was to raise public awareness about the importance
**Policy Updates**

**GAO report finds that agencies have made limited progress**

The September 2011 report of the Government Accountability Office entitled “Antibiotic Resistance: Agencies Have Made Limited Progress Addressing Antibiotic Use in Animals” examined work done by two government agencies (the Department of Health and Human Services and the U.S. Department of Agriculture) since 2004 – the data they collected on antibiotic use and resistance in food animals, the actions they took to mitigate the risk of antibiotic resistance in humans as a result of antibiotic use in animals, and the research the agencies did to pursue alternatives to antibiotics in preserving animal health. The GAO also reviewed the actions taken during this time by the EU as a whole, and Denmark in particular, to regulate antibiotic use in food animals and compared it to work done in the U.S.

The GAO found that while the HHS and USDA do collect data from pharmaceutical companies on drug sales, the data lack crucial details needed to extrapolate antibiotic use trends. For example, although bulk sales data can be obtained, the data do not show what species the antibiotics were administered to, or their intended use (e.g. disease treatment, growth promotion, etc.). Bacterial samples taken from food animals, retail meat, and industry personnel are also not collected regularly enough (some samples are only collected every 5-6 years) to show the presence and progression of antibiotic resistance over time, and is only representative of a handful of states rather than of the U.S. as a whole. Both antibiotic use data and antibiotic resistance data must be collected often and thoroughly in order to understand the relationship between degree of use and emergence of resistant bacteria in animal and human populations.

**GAO recommendations to FDA and HHS:**
- Improved data collection.
- More rigorous surveillance of resistance trends.
- Research into alternatives to antibiotics.

Since 2003, with the issuance of Guidance #152 (“Evaluating safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern”), the FDA has been regulating the use of antibiotics critically important to human medicine. If the drug treats foodborne illness and is one of only a few alternatives in treating a disease, it may not be used in ways that might jeopardize its effectiveness for human health, and the drug can be removed from the market by the FDA if that seems to be the case.

However, most antibiotics being used in food animal production today were developed before 2003, and the process of removing any of them from the market is long and expensive. The FDA instead relies on pharmaceutical companies to voluntarily phase out growth promotion as official uses of their drugs and to change their approval for sale from over-the-counter to veterinary feed directive (VFD). The FDA and HHS do not have a timeline for the phasing out of these antibiotics in food animal production, nor do they have metrics to measure their progress.

The GAO also noted that the HHS and USDA both claim to have taken steps to promote research into alternatives to antibiotics – however, they do not collect data to assess the effectiveness of these steps. Government agencies must provide funding and incentives for researching alternatives (such as vaccines), and must continually assess past research endeavors so that future efforts can be targeted more effectively to fill in any gaps. The HHS and USDA have also ended almost all uses of their drugs as a growth promoter.

Compared to the lagging U.S., the EU has raced ahead in banning the use of any antibiotic as a growth promoter. Denmark instituted this ban in 2000, followed by the entire EU in 2006. Denmark has also increased government oversight of veterinarians and food animal producers, setting limits on...
antibiotic use on farms and punishing any exceeding of the limits with additional monitoring, which the offending farm must pay for. Medically important drugs are banned for animal use except as drugs of last resort, and even then must be reported to regulatory officials when used. In turn, Denmark has also witnessed dramatic results. Salmonella has been eradicated in Denmark, antibiotic use fell 25% from 2010 to 2011, and levels of resistant *Enterococcus* (in humans) and *Campylobacter* (in animals) fell at the same time. Throughout all this, there was no corresponding increase in foodborne pathogens in retail meat.

Policymakers in the EU attribute their successes to sustained consumer interest in the issue of antibiotic resistance, constant tracking of both use data (going beyond merely tracking bulk sales data) and resistance data, and policy making based on the precautionary principle (where there is a threat of serious or irreversible damage, lack of certainty should not postpone cost-effective measures to reduce risk to human health).

Taking these evaluations into consideration, the GAO recommends that the HHS and FDA 1) collect more detailed and more nationally representative data to track the effectiveness of policies that may curb antibiotic resistance, 2) enhance surveillance of antibiotic resistant bacteria in food animals, and 3) focus federal research efforts more effectively on finding alternatives to antibiotic use. Read the full GAO report from September 2011 at www.gao.gov.

**Transatlantic report: 17 recommendations for U.S./EU collaboration**

The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was established in 2009 at the summit of the U.S. and EU presidencies, in response to the growing public health danger of antibiotic resistance and the scarcity of new drugs in the development pipeline. These simultaneous threats have led to a rise in the incidence of multi-drug resistant infections, especially in healthcare settings and in patient populations such as the elderly, the immunocompromised (as a result of HIV/AIDS, cancer, or other long illness), children, and premature infants.

In 2009, the TATFAR was charged with identifying ways that the U.S. and the EU could cooperate to address urgent issues that contribute to antibiotic resistance in three areas: 1) using antibiotics appropriately in human and veterinary medicine, 2) preventing healthcare-acquired and community-acquired infections, and 3) facilitating the development of new antibiotics. After multiple consultations with stakeholders and with the public, in September 2011 the TATFAR released their first report "Recommendations for Future Collaboration between the U.S. and the EU," containing 17 recommendations that could be implemented in the next two years.

The TATFAR came up with six recommendations pertaining to the appropriate therapeutic use of antibiotics in human and veterinary medicine. The group noted that over half of all antibiotics used in hospitals in the U.S. and the EU are prescribed unnecessarily or inappropriately, and that over half the population sampled in Europe in 2009 was fundamentally misinformed about antibiotic use (believing that antibiotics are effective against viral infections, cold, flu, etc.). These mistaken views contribute to antibiotic misuse in human healthcare and in food animal production, and the TATFAR also recognized that even when guidelines for appropriate antibiotic use are in place (antibiotic stewardship), they must develop a set of common metrics that allow guidelines to be compared between institutions and countries for evaluation and improvement.

The following recommendations were made to address appropriate antibiotic use:

- Develop a common structure and set of progress indicators for hospital antibiotic stewardship programs.
- Establish a U.S./EU working group to measure antibiotic use in hospital settings.
- Collect detailed data on the sales and use of antibiotics in food animals.
- Implement the “Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance” from the Codex Alimentarius.
- Share information on ways to promote appropriate antibiotic use in the veterinary community.
- Establish a U.S./EU working group to assess the effectiveness of communications tools in promoting behavioral change to increase appropriate antibiotic use.

The TATFAR also came up with five recommendations for preventing drug-resistant hospital-acquired and community-acquired infections. Almost all of the healthcare-associated pathogens have developed some degree of antibiotic resistance. The TATFAR’s recommendations in this area emphasized the importance of effective infection control measures and surveillance to identify reservoirs of antibiotic resistance:

- Create a point prevalence survey for healthcare-acquired infections
- Facilitate communication between the U.S. and the EU about new resistance trends
- Standardize the susceptibility reporting of bacterial isolates obtained through surveillance programs in the U.S. and the EU
- Convene public health experts to develop evaluation tools for hospital infection control programs
- Develop strategies to facilitate vaccine development for healthcare-acquired infections

The third issue, facilitating the development of new antibiotic drugs, is most hampered by the long development period (5-10 years) required to generate and perform clinical testing on a drug. The process of clinical testing on human subjects is itself extremely difficult due to the rapid progression of most bacterial diseases. The TATFAR came up with six recommendations to...
Achieve Healthy Growth. This program grant program Discover New Ways to seeking letters of inquiry for the new Deadline: January 25, 2012 Achieving Healthy Growth information on applying can be found developing non-gastrointestinal (Gut) Function and Health. The grant program Biomarkers of Gastrointestinal Function Biomarkers Foundation the Bill and Melinda Gates Grant opportunities from www.ecdc.europa.eu. Report from September 2011 at Read the full Transatlantic Taskforce continued from previous page provide incentives for drug developers and speed the process of regulatory approval and clinical testing: • Establish significant “push” incentives (e.g. more funding) and significant “pull” incentives (e.g. longer patent terms) for antibiotic drugs • Increase communication between U.S. and EU research agencies to identify opportunities for collaboration • Publicize funding opportunities between the U.S. and the EU • Facilitate the use of clinical development programs that satisfy regulatory guidelines in both the U.S and the EU • Discuss common issues in antibiotic drug development and regulation in the U.S. and the EU • Encourage information exchange on drug development, especially for resistant infections and bacterial diseases with limited treatment options. Read the full Transatlantic Taskforce Report from September 2011 at www.ecdc.europa.eu.

Grant & Training Opportunities

Grant opportunities from the Bill and Melinda Gates Foundation

Gut Function Biomarkers Deadline: January 11, 2012 (10:00 AM PST) Grand Challenges in Global Health is seeking letters of inquiry for the new grant program Biomarkers of Gastrointestinal (Gut) Function and Health. The program is committing $9 million to develop non-invasive measures of intestinal functioning as a way to assess infant health and development. More information on applying can be found at www.grandchallenges.org.

Achieving Healthy Growth Deadline: January 25, 2012 (10:00 AM PST) Grand Challenges in Global Health is seeking letters of inquiry for the new grant program Discover New Ways to Achieve Healthy Growth. This program will invest $15 million in research to discover the causes of growth faltering during the first 1000 days of life and to identify effective and affordable interventions to promote healthy growth. More information on applying can be found at www.grandchallenges.org.

Preventing Preterm Birth Initiative Deadline: January 31, 2012 The Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) is now accepting letters of inquiry for a new grant program, the Preventing Preterm Birth Initiative (PPBI). GAPPS seeks projects that explore gestational origins, biological mechanisms and the immunological response to infection and nutritional deficiency which lead to preterm birth, especially in the developing world. More information on applying can be found at gapps.org.

Rising Stars in Global Health Deadline: March 23, 2012 Grand Challenges Canada is seeking emerging innovators (within 10 years of graduation from a master’s degree or Ph.D.) from developing countries. The program is looking for innovative ideas to address complex real world challenges that involve a scientific or technological solution (new or existing) alone or in combination with social and/or business innovations. More information on applying can be found at www.grandchallenges.ca.

American Society for Microbiology (ASM): Biodefense and Emerging Diseases

Washington, D.C.: Feb 26-29, 2012 This conference will focus on research pertaining to biothreat agents, vaccines, detection and diagnostic procedures, animal and plant pathogens, biosecurity facilities, global surveillance, the training of individuals in BL3 and BL4 labs, and other vital topics.

National Institute for Animal Agriculture (NIAA) Annual Conference 2012

Denver, CO: March 26-29, 2012 This conference will focus on how decreasing resources, both natural and financial, as well as increasing regulations are making it difficult for animal agriculture to advance. With issues such as drought, tight credit, increased capital requirements, environmental regulations, more demanding animal care standards, and misinformation about how animals are raised, animal agriculture is in an important period of change.
Upcoming Opportunities and Events

**American Society for Microbiology (ASM): Candida and Candidiasis**  
*San Francisco, CA: March 29 – April 2, 2012*  
This conference will provide a forum for the Candida research community to present the most recent advances and ideas, covering a broad spectrum of subjects from clinical issues to molecular mechanisms, from growth of the fungus to response of the host, as well as tochart the course of future research and facilitate the urgent need to understand, treat, and prevent candidiasis.

**World Health Organization Forum 2012**  
*Cape Town, SA: April 24-26, 2012*  
The Council on Health Research for Development (COHRED) and the Global Forum for Health Research will focus on potentials, solutions and developing capacities, specifically in low- and middle-income countries and emerging economies, and how global collaboration can leverage this for a new era of global development support.

**American Society for Microbiology (ASM) General Meeting 2012**  
*San Francisco, CA: June 16-19, 2012*  
This conference will bring together 8,000 microbiologists in San Francisco to discuss the latest advances in the field.

**Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) General Meeting 2012**  
*San Francisco, CA: September 9-12, 2012*  
ICAAC meetings are designed to meet the needs of health care professionals, particularly physicians, clinical microbiologists, researchers, and pharmacists, specializing in infectious diseases.

**World Organization for Animal Health (OIE): Codex Committee on General Principles**  
*Paris, France: April 2-6, 2012*  
The Codex Committee will discuss food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme. The main purposes of this programme are protecting health of consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations.

**Society for Healthcare Epidemiology of America (SHEA): Advancing Healthcare Epidemiology and Antimicrobial Stewardship**  
*Jacksonville, FL: April 12-16, 2012*  
This conference will merge lectures, practical sessions, competitions, and leadership meetings to address the increasingly challenging issues in antimicrobial stewardship and demonstrate various approaches to research within the field.

**Infectious Diseases Society of America (IDSA): IDWeek**  
*San Diego, CA: October 17-21, 2012*  
IDSA’s inaugural IDWeek will feature the latest science and bench-to-bedside approaches in prevention, diagnosis, treatment, and epidemiology of infectious diseases, including HIV, across the lifespan. Partners include the Society for Healthcare Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), and the Pediatric Infectious Diseases Society (PIDS).

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